UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,254	04/30/2001	Sydney Brenner	5525-0038.10	7017

7590 11/14/2002

Iota Pi Law Group
PO Box 60850
Palo Alto, CA 94306

EXAMINER
MYERS, CARLA J

ART UNIT	PAPER NUMBER
1634	10

DATE MAILED: 11/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,254	BRENNER, SYDNEY	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *9-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. Applicants election without traverse of group I, claims 1-8, in Paper No. 9 is acknowledged.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 7 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Steffano (U.S. Patent No. 6,297,010).

Steffano teaches methods for detecting a polymorphism or mutation in a sample nucleic acid. In the method of Steffano, a reference DNA population is combined with a sample DNA population under conditions to allow for the formation of heteroduplexes between the reference and sample DNA; the heteroduplexes are treated with a 5' to 3' exonuclease which fully digests a single strand of the heteroduplexes which do not contain a mismatch, but does not fully digest heteroduplexes which contain a mismatch (i.e., a mismatch binding protein is bound to the heteroduplexes containing a mismatch and this binding protects the region containing the

mismatch from exonuclease digestion), thereby isolating the mismatched heteroduplexes from the perfectly matched duplexes; amplifying the isolated mismatched heteroduplexes; and determining the sequence of the amplified mismatched heteroduplexes in order to detect and identify the presence of a polymorphism or mutation (see, for example, column 3, column 14 (lines 63-65) and Figure 4). With respect to claims 7 and 8, Steffano teaches that the reference and sample DNA may be obtained by PCR amplification which necessarily results in the formation of subpopulations of DNA (see columns 4-6). Steffano also teaches using a reference and sample population having a complexity that allows for the rapid formation of heteroduplexes. For example, it is stated that if the polynucleotides are in excess of 1 kbp in size, the product duplex may be degraded by a double-strand cleaving activity to reduce the average size of the fragments (column 5, lines 7-10). Steffano teaches that the DNA is preferably obtained by PCR amplification and is of a length of less than about 500 base pairs (column 11). Accordingly, it is a property of the reference and sample DNA that these DNAs have complexities which permit at least ninety percent of the heteroduplexes of said subpopulations of heteroduplexes to be formed in seventy-two hours or less.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steffano in view of Weghorst (U.S. Patent No. 6,080,544).

Steffano teaches methods for detecting a polymorphism or mutation in a sample nucleic acid. In the method of Steffano, a reference DNA population is combined with a sample DNA population under conditions to allow for the formation of heteroduplexes between the reference and sample DNA; the heteroduplexes are treated with a 5' to 3' exonuclease which fully digests a single strand of the heteroduplexes which do not contain a mismatch, but does not fully digest heteroduplexes which contain a mismatch (i.e., a mismatch binding protein is bound to the heteroduplexes containing a mismatch and this binding protects the region containing the mismatch from exonuclease digestion), thereby isolating the mismatched heteroduplexes from the perfectly matched duplexes; amplifying the isolated mismatched heteroduplexes; and determining the sequence of the amplified mismatched heteroduplexes in order to detect and identify the presence of a polymorphism or mutation (see, for example, column 3, column 14 (lines 63-65) and Figure 4). Steffano (see, columns 18-19) exemplifies this method using a reference DNA population that is obtained from a cloning vector. Steffano does not exemplify methods in which both the reference and sample DNA populations are obtained from a cloning vector.

Weghorst teaches methods for identifying a polymorphism or mutation in a sample nucleic acid. In the method of Weghorst, the test and reference nucleic acids are obtained from DNA present in a cloning vector (column 15). Weghorst teaches using the same type of cloning

vector for cloning both the reference and test nucleic acids. It is noted that all cloning vectors, including the bluescript cloning vector used by Weghorst, have nucleotide sequences which constitute primer binding sites and cloning sites. Accordingly, in the method of Weghorst, the first cloning vector has a first, second and third primer binding site and a cloning site disposed between the second and third primer binding sites. The second cloning vector has a fourth and fifth primer binding site, wherein the fifth primer binding site is identical to the third primer binding site and wherein a cloning site is disposed between the fourth and the fifth primer binding sites.

In view of the teachings of Weghorst, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Steffano so as to have obtained both the test and the reference nucleic acids from cloning vectors because this would have provided an effective means for isolating and separating specific test and reference nucleic acid populations and/or of replicating and thereby increasing the quantity of the test and reference nucleic acids and thus would have provided a means for improving the sensitivity of the method for detecting the presence of a polymorphism or mutation in the test nucleic acid population.

4. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steffano in view of Weghorst and further in view of Nikiforov (cited in the IDS of Paper No. 7).

The teachings of Steffano and Weghorst are presented above. The combined references do not teach isolating the reference and test nucleic acids from a cloning vector by amplifying the

nucleic acids using a primer with a nuclease resistant 5'-end and digesting the amplified DNA with a 5' to 3' exonuclease.

Nikiforov teaches methods for detecting the presence of a polymorphism in a test nucleic acid. Nikiforov teaches that single stranded nucleic acids can be generated by amplifying a nucleic acid using a primer with a nuclease resistant 5'-end and digesting the amplified DNA with a 5' to 3' exonuclease (see page 4169).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Steffano so as to have obtained the single stranded test and reference DNA by amplifying the cloned nucleic acids using a primer with a nuclease resistant 5'-end and digesting the amplified DNA with a 5' to 3' exonuclease as taught by Nikiforov. One of ordinary skill in the art would have been motivated to have modified the method of Steffano in this manner because this would have provided an effective means for generating single stranded DNA that could be used for the formation of heteroduplexes and would have resulted in the removal of the second strand of the test and reference DNA thereby simplifying and enhancing the sensitivity of the method for detecting a polymorphism in the test DNA.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

November 12, 2002

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER